

### **REMARKS**

Reconsideration of the present application in view of the following remarks is respectfully requested. Each of claims 2, 3, 73-75 and 77-109 is currently pending and under consideration. Claims 110-116 have been withdrawn from consideration and claims 1, 4-72 and 76 have been cancelled.

As an initial matter, Applicants acknowledge and thank the Examiner for the indications in the outstanding Office Action that the finality of the last Office Action is withdrawn and that the arguments filed 12/4/2006 have been fully considered and are persuasive. The outstanding Action dated July 12, 2007, is a Non-final Action that asserts different references in support of new claim rejections.

Applicants again acknowledge and thank the Examiner for the indication in the outstanding Action that claims 83 and 84 recite allowable subject matter. The Action states that these claims are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. For the reasons stated herein, Applicants submit that the base claim and the intervening claims are also in condition for allowance, and that this objection to claims 83 and 84 is therefore moot. Withdrawal of this objection is therefore respectfully requested.

In the outstanding Action, claims 2, 3, 73-75, 77-82 and 85-106 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Vich (4,877,020) or Unicortical Dowels (University of Florida, as disclosed in applicant's specification) in view of Tucker et al. (5,674,292) in view of Heggeness et al. (5,514,180). Applicants traverse this rejection and submit that the claims are patentable over the cited combination of references.

Applicants first note for the record that U.S. Patent No. 5,674,292 to Tucker et al. is not believed to have been previously listed in an Information Disclosure Statement or in any list of references cited by the Examiner. As such, Applicants submit herewith a Supplemental Information Disclosure Statement for official entry of this reference into the record of the case.

Second, it is unclear what is meant in the Action by the citation to “Unicortical Dowels (University of Florida, as disclosed in applicant’s specification).” For purposes of this Response, it is assumed that this reference refers to the first paragraph on page 5 of the specification (Paragraph 0012 of the published application); however, further explanation regarding this citation is respectfully requested.

Of the claims rejected in the Action over this combination of references, the only independent claims are claims 73 and 94. Independent claim 73 recites a spinal spacer comprising “a cylindrical bone dowel...having impregnated therein an effective amount of a first osteogenic composition including a first substantially pure osteogenic factor.” Applicants submit that none of the cited references discloses a “substantially pure osteogenic factor” as recited in claim 73, and that none of the cited references, either alone or in combination with one another, suggests or contains any teaching that might lead a person of ordinary skill in the art to impregnate a bone dowel with an osteogenic composition including a substantially pure osteogenic factor as recited in pending claim 73.

In support of this rejection, the Action relies upon Vich as disclosing “a spinal spacer for insertion into a disc space between adjacent vertebrae comprising a cylindrical dowel configured for engagement with a concave space in the adjacent vertebrae.” (Office Action, pages 3-4). The Action acknowledges that “Vich fails to disclose the combination of osteogenic composition being impregnated with substantially pure osteogenic factor,” but asserts that “Tucker et al teaches impregnating porous bone with osteogenic factor, including bone morphogenic proteins.” (Office Action page 4). Applicants traverse this assertion on the grounds that it incorrectly interprets the teachings of Tucker et al. Tucker et al. fails to support rejection of the identified claims under Section 103 for at least the following two reasons: (1) Tucker et al. does not disclose impregnation of an osteogenic factor (or any other substance) into a bone dowel (or any other intact bone component), and (2) there is no disclosure in Tucker et al of any “osteogenic composition including a first substantially pure osteogenic factor” as recited in independent claim 73.

Tucker et al. describes a method for sterilizing a device that includes “osteogenic proteins,” and purports to describe a method that sterilizes such a device without denaturing the proteins. While Tucker et al. does not describe the method as being limited by the specific mechanical features of the device, Tucker et al. specifies that the devices include “a biologically active protein, for example, an osteogenic protein, in combination with an insoluble carrier material.” (See Column 2, lines 5-7). For purposes of clarity, Applicant would draw the Examiner’s attention to the fact that the term “carrier material” is used interchangeably in Tucker et al. with the term “carrier matrix material” to refer to a “three dimensional structure sufficient to act as a scaffold for infiltrating and proliferating cells...” (See Column 8, lines 21, et seq.). The matrix is further described in Tucker et al. as follows:

The matrix can comprise a shape-retaining solid made of loosely adhered particulate material, e.g., with collagen. It also can comprise a molded, porous solid, or simply an aggregation of close-packed particles held in place by surrounding tissue. The matrix further can comprise an insoluble, non-particulate solid with interstices sufficient to allow the attachment and proliferation of infiltrating cells. (Column 8, lines 49-55).

Tucker et al. teaches away from the subject matter of pending claim 73, which recites a “bone dowel having [the osteogenic composition] impregnated therein.” While the carrier material described in Tucker et al. can be a piece of bone, Tucker et al. does not describe a piece of bone that has an osteogenic protein impregnated therein as recited in claim 73 of the present application. Rather, Tucker et al. discloses that if the carrier material is bone, the osteogenic protein is coated on the surface of the bone. The only mention in Tucker et al. of a device that includes a segment of intact (i.e., non-pulverized) bone such as a bone dowel, is found at Column 8, lines 58-63, as follows:

Large allogenic bone implants also can act as a carrier for the matrix if their marrow cavities are cleaned and packed with carrier and the dispersed osteogenic protein. Alternatively, the bone implants may act as a carrier per se and in such cases the osteogenic protein may be coated directly onto the surface of the bone implant. (emphasis added).

The first statement in the above-quoted portion of the Tucker et al. specification uses the word “carrier” twice to refer to two different parts of the device of that embodiment. The first occurrence of the word “carrier” in that statement refers to the operation of the bone implant in the described embodiment as a type of container for an osteogenic material. The bone implant is not a “carrier matrix” in that embodiment as that term is used in the Tucker et al. specification, but rather operates as a container for holding the “carrier matrix”/osteogenic protein material. As such, in the described embodiment, the bone implant is clearly not impregnated with an osteogenic composition as recited in pending claim 73, but rather acts as a container for holding the “carrier matrix”/osteogenic protein material.

The second statement in the above-quoted portion of the Tucker et al specification is believed to be the only suggestion that can be found in Tucker et al. of the use of a “[l]arge allogenic bone implant” itself as a carrier, i.e., as the “carrier matrix” for an osteogenic protein. However, the Examiner will appreciate that this embodiment also does not disclose impregnating the bone with an osteogenic composition as recited in pending claim 73, but rather states that “the osteogenic protein may be coated directly onto the surface of the bone implant.” (emphasis added).

Taking the teachings of Tucker et al. as a whole, it is apparent that this reference teaches away from a bone dowel impregnated with an osteogenic composition as recited in pending claim 73 because, although many embodiments are described in which an osteogenic protein is imbedded in or otherwise entrained in a carrier matrix, the only mention of using a section of bone as a carrier matrix states that the osteogenic protein is coated on its surface. A person of ordinary skill in the art at the time the present application was filed would understand this to teach away from the subject matter recited in pending claim 73. As such, Applicants submit that Tucker et al. does not disclose impregnating a bone dowel with an osteogenic factor, would not motivate a person of ordinary skill in the art to do so, and cannot support the rejection of claim 73 under Section 103.

Turning now to the recitation in claim 73 of an “osteogenic composition including a first substantially pure osteogenic factor,” the cited art also does not disclose any such

composition and, indeed, the Office Action does not identify any reference that discloses this feature. Rather than pointing to any prior art disclosure, the Action addresses the absence of the claimed subject matter in the cited art by asserting that Applicants' own specification somehow operates as an admission that "suffices in meeting applicant's claimed limitation." (Office Action, Page 4). In support of this position, the Action states that:

- (1) Applicant's specification...indicates that the osteogenic factors may be prepared by one skilled in the art;
- (2) Applicant's own specification fails to provide further disclosure regarding the claimed feature of "substantially pure osteogenic factor";
- (3) Applicant's specification fails to further elaborate on what constitutes "substantially pure";
- (4) Applicant's specification is devoid of any further processing of the factor, beyond what applicant disclosed to be prior art; and
- (5) Applicant must rely on the disclosure of others in the field to support and/or give meaning to the "metes and bounds" of the recitation of "substantially pure."

The Action then asserts on the basis of the above that the Applicants have somehow made an admission that the "prior art suffices in meeting applicant's claimed limitation." In reply, Applicants submit that (1) this reasoning fails to constitute an admission of prior art for several reasons, and (2) even assuming *arguendo* that the prior art discloses a "substantially pure osteogenic factor," the Action does not identify any disclosure in the cited art that discloses the combination of such a substantially pure osteogenic factor with the other elements recited in claim 73.

First, Applicants have made no admission that a "substantially pure osteogenic factor" is prior art, and the reasoning set forth at Page 4 of the Action does not support an assertion that Applicants made an admission of prior art. Moreover, the Action does not make clear the nature of the alleged "disclosure of others in the field" that is referred to in item 5 above, nor any legitimate manner in which the alleged "disclosure of others" or its use to interpret claim language can support the assertion in the Action that Applicants have made an admission of prior art.

Putting aside for the moment the question of the nature of the “disclosure of others” references in item 5 above, the assertion is incorrect because the meaning of the words “substantially pure” in pending claim 73 does not necessarily “rely on the disclosure of others.” Rather, the meaning of the words “substantially pure” in pending claim 73 is a question of claim interpretation. Claim interpretation does not depend on, or turn on, a “disclosure of others,” but rather is based upon the understanding of a person of ordinary skill in the art at the time the patent application is filed. It is axiomatic that interpretation of terms in a patent claim is based upon what a person of ordinary skill in the art at the time of the application would understand the terms to mean. In this regard, Section 2111.01 of the Manual of Patent Examining Procedure (“MPEP”) states the following:

"[T]he ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313<, 75 USPQ2d 1321>, 1326< (Fed. Cir. 2005) (en banc). *Sunrace Roots Enter. Co. v. SRAM Corp.*, 336 F.3d 1298, 1302, 67 USPQ2d 1438, 1441 (Fed. Cir. 2003); *Brookhill-Wilk 1, LLC v. Intuitive Surgical, Inc.*, 334 F.3d 1294, 1298 67 USPQ2d 1132, 1136 (Fed. Cir. 2003) ("In the absence of an express intent to impart a novel meaning to the claim terms, the words are presumed to take on the ordinary and customary meanings attributed to them by those of ordinary skill in the art."). It is the use of the words in the context of the written description and customarily by those skilled in the relevant art that accurately reflects both the "ordinary" and the "customary" meaning of the terms in the claims. *Ferguson Beauregard/Logic Controls v. Mega Systems*, 350 F.3d 1327, 1338, 69 USPQ2d 1001, 1009 (Fed. Cir. 2003)

The meaning of the terms “substantially pure” in claim 73 is properly based upon what a person of ordinary skill in the art at the time of the application would understand these terms to mean, and it is improper for the Action to assert that the meaning of these terms is dependent upon some unidentified prior art disclosure.

Furthermore, there is no authority identified in the Action that supports the proposition that information used to interpret claim terms can be interpreted as an admission

by Applicants. Applicants respectfully request that the Examiner identify any such authority if this grounds for rejecting claims is maintained in a subsequent Action.

Turning to the question of the nature of the “disclosure of others” referenced in item 5 above, the Action cites no reference and provides no explanations that would give meaning to this phrase. Taking the statement in context and, in particular, in view of the immediately preceding sentence at Page 4 of the Action, it appears that the Action is referring to a disclosure that describes a method for “further processing” an osteogenic factor to make a “substantially pure osteogenic factor.” Applicant submits, however, that no such disclosure is needed to give meaning to the words “substantially pure,” nor is any such disclosure needed to enable a person of ordinary skill in the art to practice the claimed invention. For example, at the time the application was filed, a person of ordinary skill in the art would have understood upon reading the present specification that a substantially pure osteogenic factor could be synthesized using known protein synthesis techniques. At the time the application was filed a variety of osteogenic factors had been isolated from natural sources and had been characterized. While such osteogenic factors isolated from natural sources may not be “substantially pure,” a person of ordinary skill in the art armed with information regarding the characterization of osteogenic factors, such as amino acid sequences and three-dimensional structures of the factors, would be able to synthesize a substantially pure osteogenic factor to be used as described and claimed in the present application. Furthermore, while the specification enables the practice of the subject matter recited in the claim, the motivation to make the claimed combination comes only from the present specification, and would not have been obvious in view of any prior disclosure of others.

Moreover, the Action does not identify any “disclosure of others in the field,” but rather relies upon an assumption that there exists some such disclosure. If a disclosure exists that supports a rejection of claims, such disclosure must be made of record so that its effect on the patentability of the pending claims, if any, can be evaluated. If no such disclosure exists, Applicants submit that it is improper for the Action to assert it for any reason, much less for purpose of alleging an admission of prior art. Moreover, Applicants submit that,

even if a prior art disclosure were to be identified that describes a process for purifying a prior art osteogenic factor to produce a substantially pure osteogenic factor, or for synthesizing a substantially pure osteogenic factor, such a disclosure still does not anticipate or render obvious the combination recited in claim 73, and cannot properly be used to support an assertion that Applicants made an admission that the “prior art suffices in meeting applicant’s claimed limitation,” as asserted in the Action.

In view of the above remarks, Applicants submit that independent claim 73 is patentable over the cited combination of references, and respectfully requests an indication that claim 73 is allowed.

Claims 2, 3, 74-75 and 77-93 depend, either directly or indirectly, from independent claim 73. Applicants submit that these dependent claims recite patentable subject matter for at least the same reasons that the subject matter of independent claim 73 is patentable, and for other reasons. For example, claim 77 is dependent on claim 73 and specifies that “said osteogenic factor is a recombinant human protein.” Claim 78 is dependent upon claim 77 and further specifies that “said osteogenic factor is rhBMP-2, rhBMP-4, rhBMP-7 or a mixture or heterodimer thereof.” The only statement made in the Office Action relating to the rejection of these claims is the following: “see column 10, lines 49+ of Heggeness et al.” In traversal of this rejection, Applicants would draw the Examiner’s attention to the fact that the cited reference does not disclose any recombinant human protein, and does not disclose “rhBMP-2, rhBMP-4, rhBMP-7 or a mixture or heterodimer thereof.” Therefore, the references of record fail to support a rejection of claims 77 and 78 in the present case for this further reason that none of the cited references, even if properly combined, teaches or suggests the use of a “recombinant human protein” or “rhBMP-2, rhBMP-4, rhBMP-7 or a mixture or heterodimer thereof.” Applicants respectfully request an indication that claims 77 and 78 are allowed.

Claim 82 is dependent upon claim 80, which is in turn dependent on claim 73. Claim 82 specifies that “said bone dowel is obtained from the diaphysis of a long bone having a medullary canal” and that the spacer further comprises “an effective amount of a second



osteogenic composition to stimulate osteoinduction, said second composition packed within said chamber.” The only basis for the rejection of claim 82 provided in the Office Action is the following: “[S]ee column 10-11 of Heggeness, et al. Note the claimed combination of the first and second osteogenic [sic] material does not preclude that both materials be present in the same matrix and packed in the chamber.” In traversal of this rejection, Applicants believe that the above-quoted assertion in the Action reflects an erroneous interpretation of claim 82. This claim encompasses a bone dowel in which a “first osteogenic composition” is impregnated in the bone dowel and a “second osteogenic composition” is packed in the chamber. Thus, while more than one osteogenic material can be “present in the same matrix and packed in the chamber,” claim 82 recites that the “first osteogenic composition” is impregnated in the bone dowel. Therefore, the Examiner’s rationale, to the extent it is understood by Applicants, does not support a rejection of claim 82. The cited art does not disclose a bone dowel having an osteogenic composition impregnated therein (as discussed above), much less a bone dowel having an osteogenic composition impregnated therein AND a second osteogenic composition positioned in a chamber defined in the dowel. Applicants therefore submit that the asserted rejection of claim 82 must be withdrawn for this further reason. Applicants respectfully request an indication that claim 82 is allowed.

The only comment in the outstanding Office Action in support of the rejection of claims 86 and 87 is the following: “see figure 1 of Vich.” Each of claims 86 and 87, however, recites features that are not shown in figure 1 of Vich. For example, claim 87 recites a bone dowel with an outer surface defining a thread “including plurality of teeth each tooth of the plurality of teeth having a crest between a leading flank and an opposite trailing flank [and] wherein said crest of each said tooth is flat.” Figure 1 of Vich does not disclose a bone dowel including these features and therefore cannot support a rejection of these claims. Applicants respectfully request withdrawal of the rejection of claims 86 and 87 and an indication that these claims are allowed.

The only comment in the outstanding Office Action in support of the rejection of claims 91 and 92 is the following: “see column 8, lines 55+ of Brekke.” Claim 91 is

dependent upon claim 90, which is in turn dependent on claim 73. Claim 91 recites that “said first osteogenic factor is provided in a pharmaceutically acceptable carrier [and] said carrier is physiological saline.” Claim 92 is also dependent upon claim 90, which is in turn dependent on claim 73. Claim 92 recites that “said first osteogenic factor is provided in a pharmaceutically acceptable carrier [and] said carrier is buffered sterile water.”

Brekke describes an osteogenic bone graft substitute device composed of a porous plastic component made of polylactic acid and hyaluronic acid polymers. Brekke discloses that, immediately prior to implantation of the porous plastic device, a liquid solution or suspension of bone morphogenetic protein and bone derived growth factor is injected into cavities in the plastic using a syringe. The reasoning set forth in the Office Action requires that the liquid in which the bone morphogenetic protein and bone derived growth factor are suspended, which can be sterile water, plasma or serum, is considered to operate as a “carrier” for the bone morphogenetic protein and bone derived growth factor, and the Action suggests that the liquid could be substituted for the “carrier materials” in the devices described by Heggeness et al. and Tucker et al. In traversal, Applicants submit that this combination is improper under Section 103 because a device resulting from this combination would be inoperable for its intended purpose. A person of ordinary skill in the art at the time the present application was filed would have well understood that the “carrier materials” and “carrier matrix materials” described by Heggeness et al. and Tucker et al. must have physical/mechanical properties suitable to provide a scaffold for bony ingrowth after implantation, to hold the osteogenic factors, and in embodiments pertinent to the present application to provide structural support to the adjacent bone. Thus, the only component in Brekke that could be considered analogous to a “carrier material” of Heggeness et al. and Tucker et al. is the porous plastic component described in Brekke. If any of the carrier materials described in Heggeness et al. and Tucker et al. were substituted with the liquid disclosed in Brekke, the resulting materials would not be operable to achieve the intended result, i.e., to provide a “scaffold for bony ingrowth” and mechanical support for adjacent bony portions. Applicants therefore submit that the combination of references asserted in the

Action does not support a rejection of claims 91 or 92 under Section 103 of the Patent Statute, and respectfully request an indication that claims 91 and 92 are allowed.

In support of a rejection of claim 93, the Action generally refers to Figure 26 of Heggeness et al. and generally refers to the “carrier as taught by Tucker et al.”; however, it is not clear what part of Figure 26 of Heggeness et al. or what part of the disclosure of Tucker et al. discloses a device in which a “carrier is provided as a sponge, strip, or a sheet,” as recited in claim 93. It is submitted that the Action does not provide sufficient explanation to support the rejection of this claim, and it is believed that the cited references do not teach or disclose a device having the claimed features. Applicants therefore respectfully request an indication that claim 93 is allowed.

The second independent claim pending in the present application is claim 94. Applicants submit that independent claim 94 is also in condition for allowance. The references of record fail to support a rejection of claim 94 at least because none of the cited references teaches or suggests “an osteogenic composition including a substantially pure osteogenic factor” (as discussed above). Furthermore, Applicants traverse the assertion in the Action that the Applicants have made an admission of prior art for the reasons described above. None of the cited references teaches or suggests the use of a “substantially pure osteogenic factor” in any manner, much less in connection within a dowel comprising bone graft, as recited in claim 94. Applicants therefore respectfully request withdrawal of the asserted rejection of claim 94, and submit that claim 94 is in condition for allowance.

Claims 95-116 depend, either directly or indirectly, from independent claim 94. Applicants submit that these dependent claims recite patentable subject matter for at least the same reasons that the subject matter recited in independent claim 94 is patentable, and for other reasons. The only rationale provided in the Action for the rejection of claims 96-106 is that, “Dependent claims 96-106 generally corresponds [sic] to the dependent claims 2, 3, 74-93 supra and are similarly rejected accordingly.” In traversal of this rejection, Applicant notes that (1) several of claims 96-106 do not have corresponding claims in claims 2, 3 and 74-93, and (2) to the extent that some of claims 96-106 correspond to one or more of claims

2, 3, and 74-93, the claims are in condition for allowance for the same reasons that claims 2, 3 and 74-93 are in condition for allowance, discussed above. Applicants would specifically draw the Examiner's attention to the fact that claims 100, 101, 102 and 103 have no corresponding claim in claims 2, 3 and 74-93. As such, the Action provides no rationale supporting the rejection of these claims, and Applicant's respectfully request an indication that these claims are allowed.

Dependent claims 107-109 are rejected in the outstanding Action over a different combination of references including the above-cited references and an additional reference (Bianchi). While Applicants believe that this combination also fails to teach or suggest the subject matter recited in claims 107-109 for the same reasons that the cited references fail to teach or suggest the subject matter recited in independent claim 94, as amended, Applicants also submit that U.S. Patent No. 6,033,438 to Bianchi does not qualify as prior art that can be cited against the pending claims. It is noted that the Bianchi patent was filed on June 3, 1997. The present application is a continuation application, and it claims priority to multiple applications in a line of cases extending back to an original parent application filed October 16, 1995. Notable for purposes of the present discussion is that the present application claims priority to Application No. 08/740,031 filed on October 23, 1996 and is therefore entitled to at least this date as its effective filing date for purposes of determining qualification of references as prior art. Since the Bianchi patent was filed after this date, the Bianchi patent does not qualify as prior art to the present application. Accordingly, Applicants respectfully request withdraw of the rejection of claims 107-109 under 35 U.S.C. § 103(a) as being unpatentable over this combination of references.

Claims 110-116 have been withdrawn from consideration on the grounds that they are drawn to a nonelected species and that there is no allowable generic or linking claim. Applicants respectfully request that claims 110-116 be reinstated and allowed on the bases that independent claim 94 is allowable and that claims 110-116 recite subject matter that satisfies all statutory requirements for patentability.

In view of the foregoing remarks, Applicants respectfully submit that none of the rejections asserted in the outstanding Action can properly be maintained. Accordingly, reconsideration leading to withdraw of all the rejections under 35 U.S.C. § 103(a) and allowance of this application containing claims 2, 3, 73-75 and 77-116 are respectfully requested.

**Conclusion**

In view of the above, Applicants respectfully submit that the rejections stated in the outstanding Action are overcome and that the present application is in condition for allowance. Action to that end is respectfully requested. If there are any remaining issues that can be addressed telephonically, the Examiner is invited to contact the undersigned to discuss the same. Nothing in this document is intended to be an admission that any of the cited references qualifies as prior art or that the arguments in support of patentability presented herein are the only reasons that the claims are in condition for allowance. Rather, Applicants expressly reserve the right to make showings at a later time to remove/disqualify one or more references from the prior art, if appropriate, and/or to present additional arguments in favor of patentability of the pending claims over the cited references.

Respectfully submitted,

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